In view of the regional differences in sensitivity found in the earlier experiments one would expect that the units responding, for example, to acetone would be found more often in the front part of the bulb and those responding to heavy oil at the back. There is undoubtedly a segregation of this kind, although, in the middle region, unit discharges have been obtained with substances from all the groups. It is true that most of these units can be made to discharge to a wide range of stimuli if the concentration is raised, but there will always be outlying parts of the olfactory organ where it has the threshold value needed to bring out the differential effects.

Assessment of the Different Factors

A great deal remains to be done before we can assess the different factors concerned in olfactory discrimination, but the important point is that neighbouring groups of olfactory receptors have marked differences in their sensitivity to different smells. I have no doubt, therefore, that olfactory discrimination is not due solely to the complex structure of the organ—that is, to the deposition of the material in different patterns on its surface owing to differences in the rate of air flow, size of molecules, etc.

In fact the olfactory epithelium proves to be a large collection of nerve cells which look alike, apart from the position of the nucleus, but differ so much in their properties that some will be excited by a trace of acetone vapour and others by a trace of benzene. This, of course, is no more than would be expected by anyone who contemplates the remarkable discriminative power of the nose. But it is an important point to have established, and I do not regret the time I have spent in trying to develop a different hypothesis.

It may be that the point is important only in connexion with the working of the olfactory organ; the receptors there may be the only cells which have developed such a high degree of chemical discrimination. But nerve cells in other places may show traces of the same discriminative power. Let us suppose, then, that there are sheets of such cells in the central nervous system with dendrites ending freely amongst the dendrites of afferent neurones, so that material liberated from these might come into contact with the dendrites from more than one cell. It cannot be expected that the terminations of the afferent neurones would liberate molecules as different as acetone and benzene, but if some neurones liberate acetylcholine and some noradrenaline it is not impossible that the molecules liberated by the fibre from a temperature receptor might differ considerably from those liberated by a pain fibre. The ultimate destination of the different signals reaching the dendritic network would then be determinated by the different chemical sensitivities of the neurones whose dendrites are stimulated.

It is perhaps worth pointing out that the excitation of an olfactory receptor is a rapid process which ceases usually at the end of inspiration when the delivery of vapour is suspended, that the number of molecules needed to excite must be very small, and that they must be removed or neutralized rapidly. The same could be said of the excitation of a nerve cell by a humoral transmitter. I am bound to admit the difficulty of believing that all the different groups of molecules which stimulate the olfactory receptors are dealt with by different specific enzymes, as cholinesterase deals with acetylcholine, but they are certainly inactivated rapidly and completely.

Speculations which cannot be put to experimental test are seldom worth elaborating, and I cannot pretend that we should be in a much better position if this speculation turned out to be correct. A selective transmission determined by the nature of the material set free in the dendritic network might allow more variation than one determined by the detailed connexion of dendrites, but that is all that can be claimed for it.

Yet I think the olfactory organ may have something to teach us about the organization of the nervous system. Since its nerve cells are found to have such selective properties we must be ready to look for similar properties in nerve cells elsewhere.

Conclusion

That, I am afraid, is a poor conclusion to a lecture which commemorates a man whose researches were of such immediate practical benefit to so many people. I wish I had something better to offer than these incomplete results on a sense organ which has never roused much interest. I can still recall the intense interest which the work of Banting and Best aroused in all of us, in physiologists as well as in every doctor. But such triumphant victories come very rarely, and they are separated by the slow, plodding attack on a wide front. I have described a minor incident in that attack with a speculation attached to it; but I have done so because most of our research is like that, and because it is with such inconclusive results that you must contrast the spectacular advance which came with the finding of insulin.

PROTECTION AFFORDED BY SICKLE-CELL TRAIT AGAINST SUBTERTIAN MALARIAL INFECTION

BY

A. C. ALLISON, D.Phil., B.M.*

(From the Clinical Pathology Laboratory, the Radcliffe Infirmary, Oxford)

The aetiology of sickle-cell anaemia presents an outstanding problem common to both genetics and medicine. It is now universally accepted that the sickle-cell anomaly is caused by a single mutant gene which is responsible for the production of a type of haemoglobin differing in several important respects from normal adult haemoglobin (Pauling *et al.*, 1949; Perutz and Mitchison, 1950). Carriers of the sickle-cell trait who are heterozygous for the sickle-cell gene have a mixture of this relatively insoluble haemoglobin and normal haemoglobin; hence their erythrocytes do not sickle *in vivo*, whereas some at least of the homozygotes, who have a much greater proportion of sickle-cell haemoglobin, have sickle cells in the circulating blood, with inevitable haemolysis and a severe, often fatal, haemolytic anaemia. There is also a much smaller group of sickle-cell anaemia patients who are heterozygous for the sickle-cell gene as well as for some other hereditary abnormality of haemoglobin synthesis (Neel, 1952).

It is thus possible to approach the problem from the clinical or the genetical side. From the clinical point of view it is important to distinguish between carriers of the sickle-cell trait who show no other haematological abnormalities and patients with sickle-cell anaemia, who have a haemolytic disease which can reasonably be attributed to sickling of the erythrocytes. From the genetical point of view the main distinction is to be drawn between those who are homozygous and those who are heterozygous for the sickle-cell gene. In the great majority of instances two classifications coincide—that is, most individuals with the sickle-cell trait are heterozygous and most cases of sickle-cell anaemia, in Africa at least, are homozygous for the sickle-cell gene.

*Staines Medical Research Fellow of Exeter College, in receipt of a grant from the Medical Research Council.

The sickle-cell trait is remarkably common in some parts of the world. Among many African negro tribes 20% or more of the total population have the trait, and frequencies of 40% have been found in several African tribes (Lehmann and Raper, 1949; Allison, 1954). In parts of Greece frequencies of 17% have been described (Choremis *et al.*, 1953), and as many as 30% of the population in Indian aboriginal groups are affected (Lehmann and Cutbush, 1952).

Wherever the sickle-cell trait is known to occur sickle-cell anaemia will also be found. For a time it was thought by some workers that sickle-cell anaemia was rare among African negroes, but so many cases have been described during the past few years that this view is no longer tenable (Lambotte-Legrand and Lambotte-Legrand, 1951; Foy *et al.*, 1951; Edington, 1953; Vandepitte and Louis, 1953).

The main problem can be stated briefly: how can the sickle-cell gene be maintained at such a high frequency among so many peoples in spite of the constant elimination of these genes through deaths from the anaemia? Since most sickle-cell anaemia subjects are homozygotes, the failure of each one to reproduce usually means the loss of two sickle-cell genes in every generation. It can be estimated that for the lost genes to be replaced by recurrent mutation so as to leave a balanced state, assuming that the sickle-cell trait—that is, the heterozygous condition—is neutral from the point of view of natural selection, it would be necessary to have a mutation rate of the order of 10^{-1}. This is about 3,000 times greater than naturally occurring mutation rates calculated for man and, with rare exceptions, in many other animals—3.2×10^{-5} in the case of haemophilia (Haldane, 1947). A mutation rate of this order of magnitude can reasonably be excluded as an explanation of the remarkably high frequencies of the sickle-cell trait observed in Africa and elsewhere.

Possibility of Selective Advantage

Of the other explanations which can be advanced to meet the situation, one has received little attention: the possibility that individuals with the sickle-cell trait might under certain conditions have a selective advantage over those without the trait. It was stated for many years that the sickle-cell trait was in itself a cause of morbidity, but this belief seems to have been based upon unsatisfactory criteria for distinguishing the trait from sickle-cell anaemia. The current view is that the sickle-cell trait is devoid of selective value. Henderson and Thornell (1946) found that in American negro air cadets who had passed a searching physical examination the incidence of the sickle-cell trait was the same as in the general negro population of the United States. Lehmann and Milne (1949) were unable to discover any correlation between haemoglobin levels and the presence or absence of the sickle-cell trait in Uganda Africans. And Humphreys (1952) could find no evidence that the sickle-cell trait was responsible for any morbidity in Nigerian soldiers.

However, during the course of field work undertaken in Africa in 1949 I was led to question the view that the sickle-cell trait is neutral from the point of view of natural selection and to reconsider the possibility that it is associated with a selective advantage. I noted then that the incidence of the sickle-cell trait was higher in regions where malaria was prevalent than elsewhere. The figures presented by Lehmann and Raper (1949) for the frequency of the sickle-cell trait in different parts of Uganda lent some support to this view, as did the published reports from elsewhere. Thus the trait is fairly common in parts of Italy and Greece, but rare in other European countries; in Greece the trait attains its highest frequencies in areas which are conspicuously malarious (Choremis *et al.*, 1951).

Relation between Malaria and Sickle-cell Trait

Other reports appeared suggesting more directly that there might be a relationship between malaria and the sickle-cell trait. Beet (1946) had observed that in a group of 102 sicklers from the Balovale district of Northern Rhodesia only 10 (9.8%) had blood slides showing malaria parasites, whereas in a comparable group of 491 non-sicklers 75 (15.3%) had malaria parasites. The difference in incidence of malaria in the two groups is statistically highly significant ($\chi^2=19.349$ for 1 d.f.)*; hence Beet's figures imply strongly that malaria is less frequent among individuals with the sickle-cell trait than among those without the trait. The difference in malarial susceptibility between sicklers and others seemed to be most pronounced at the time of the year when malaria transmission was lowest.

Later, in the Fort Jameson district of Northern Rhodesia, Beet (1947) found that the same difference was present, although it was much less pronounced. Of 1,019 non-sicklers, 312 (30.6%) had blood slides with malaria parasites, whereas of 149 sicklers 42 (28.2%) showed malaria parasites. This difference is not statistically significant. However, among the sicklers from Fort Jameson enlarged spleens were less common than among non-sicklers. In a series of 569 individuals there were 87 with the sickle-cell trait; 24 (27.9%) of these had palpable spleens, as compared with 188 (39.0%) with splenomegaly out of 482 non-sicklers. This difference is again statistically significant ($\chi^2=4.11$ for 1 d.f.). Beet concluded that Africans with the sickle-cell trait were probably liable to recurrent attacks of thrombosis, with resultant shrinkage of the spleen.

Brain (1952a), also working in Rhodesia, confirmed Beet's observation that the spleen is palpable in a much lower proportion of sicklers than of non-sicklers; he went on to suggest that the finding might be explained by diminished susceptibility to malaria on the part of the sicklers. Moreover, Brain (1952b) compared the proportion of hospitalized cases in groups of African mine-workers with and without the sickle-cell trait. He found that the sicklers actually spent less time in hospital, on an average, than did the control group of non-sicklers. The incidence of malaria and pyrexias of unknown origin was much lower in the group with sickle cells.

It became imperative, then, to ascertain by more direct methods of investigation whether sickle cells can afford some degree of protection against malarial infection, thereby conferring a selective advantage on possessors of the sickle-cell trait in regions where malaria is hyperendemic. An opportunity to do this came during the course of a visit to East Africa in 1953.

Incidence of Malarial Parasitaemia in African Children with and without the Sickle-cell Trait

The observations of Beet and of Brain on differences in parasite rates and spleen rates are open to criticism because the populations were heterogeneous and were drawn from relatively wide areas. It was decided, therefore, to carry out similar tests on a relatively small circumscribed community, where all those under observation belong to a single tribe. Children were chosen rather than adults as subjects for the observations so as to minimize the effect of acquired immunity to malaria. The recorded incidence of parasitaemia in a group of 290 Ganda children, aged 5 months to 5 years, from the area surrounding Kampala (excluding the non-malarious township) is presented in Table I. The presence of sickling was demonstrated by chemical reduction of blood with isotonic sodium metabisulphite (Daland and Castle, 1948). Fresh reducing solutions were made up daily.

*These and other statistics in this paper are my own, using available figures.

TABLE I

	With Parasitaemia	Without Parasitaemia	Total
Sicklers	12 (27·9%)	31 (72·1%)	43
Non-sicklers ..	113 (45·7%)	134 (53·3%)	247

It is apparent that the incidence of parasitaemia is lower in the sickle-cell group than in the group without sickle cells. The difference is statistically significant ($\chi^2=5.1$ for 1 d.f.). In order to test as many families as possible only one child was taken from each family. There is no reason to suppose that these groups are not comparable, apart from the presence or absence of the sickle-cell trait.

The parasite density in the two groups also differed : of 12 sicklers with malaria, 8 (66.7%) had only slight parasitaemia (group 1 on an arbitrary rating), while 4 (33.3%) had a moderate parasitaemia (group 2). Of the 113 non-sicklers with malaria, 34% had slight parasitaemia (group 1), the parasite density in the remainder being moderate or severe (group 2 or 3).

It may be noted, incidentally, that of the four cases in the sickle-cell group with moderate parasitaemia three had *P. malariae*, even though this species is much less common than *P. falciparum* around Kampala. It seems possible from these and other observations that the protection afforded by the sickle-cell trait is more effective against *P. falciparum* than against other species of plasmodia, but much further work is necessary to decide the point.

These results suggest that African children with the sickle-cell trait have malaria less frequently or for shorter periods, and perhaps also less severely, than children without the trait. Further evidence regarding the protective action of the sickle-cell trait could be obtained only by direct observation on the course of artificially induced malarial infection in volunteers.

Progress of Malarial Infection in Adult Africans with and without the Sickle-cell Trait

Fifteen Luo with the trait and 15 Luo without the trait were accepted for this investigation. All the volunteers were adult males who had been away from a malarious environment for at least 18 months. The two groups were of a similar age and appeared to be strictly comparable apart from the presence or absence of the sickle-cell trait. Two strains of *P. falciparum* were used—one originally isolated in Malaya and one from near Mombasa, Kenya ; in Table II these are marked with the subscripts 1 and 2 respectively. The infection was introduced by subinoculation with 15 ml. of blood containing a large number of trophozoites (B in the table) or by biting with heavily infected *Anopheles gambiae* (M in the table). At least 3 out of the 10 mosquitoes applied had bitten each individual, and the presence of sporozoites was confirmed by dissection of the mosquitoes.

The cases were followed for 40 days. Parasite counts for each case were made by comparison with the number of leucocytes in 200 oil-immersion fields of thick films, the absolute leucocyte counts being checked at intervals. The abbreviated results of these counts are shown in Table II. In the few cases in which parasitaemia was pronounced and the symptoms were relatively severe the progress of the disease was arrested. At the end of the period of observation in every case a prolonged course of antimalarial chemotherapy was given.

Discussion

It is apparent that the infection has become established in 14 cases without the sickle-cell trait. The parasitaemia is relatively light, however, when compared with that observed in non-immune populations—for example, the Africans described by Thomas *et al.* (1953). This is to be expected : the Luo come from a part of the country where malaria is hyperendemic, and they have acquired a considerable immunity to malarial infection in childhood. This factor makes the interpretation of the observations rather more difficult ; however, it could not be avoided, since all the East African tribes who have high sickling rates come from malarious areas, and the acquired immunity should operate with equal force in the groups with and without sickle-cells. The acquired immunity was actually an advantage, since the symptoms were mild and the chances of complication very slight.

In the group with sickle cells, on the other hand, the malaria parasites have obviously had great difficulty in establishing themselves, in spite of repeated artificial infec-

TABLE II

No.	Mode of Infection and Strain	Day after Infection: 8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40
Luo With No Sickle-cells																		
1	M_2 B_1	0·03	—	0·07	2·5	5·0	2·5	5·0	1·2	0·4	0·02	0·01	—	—	0·1	0·01	0·01	ST
2	M_2 B_1	—	—	—	—	—	—	—	0·03	0·13	0·41	—	—	—	—	0·03	—	ST
3	M_2 B_1	—	—	—	—	—	—	—	0·1	0·02	0·20	5·0	2·5	1·25	1·67	0·2	5·0	2·0 S
4	M_2 B_1	—	—	—	—	0·02	0·02	0·5	0·83	0·12	0·2	1·0	1·0	0·83	0·25	0·17	—	ST
5	M_2 B_2	—	—	—	—	0·05	1·0	1·67	0·25	0·05	0·07	0·25	1·2	1·0	0·03	—	—	ST
6	B_1	0·02	5·0	10·0	10·0	1·0	0·1	0·01	ST	—	—	—	—	—	—	—	—	—
7	B_2	—	—	—	—	15·0	50·0	ST	—	—	—	—	—	—	—	—	—	—
8	B_2	—	—	0·13	5·0	1·67	0·33	—	—	ST	—	—	—	—	—	—	—	—
9	B_1	—	—	—	—	5·0	—	0·1	0·5	2·5	—	1·0	0·1	2·5	10·0	5·0	0·5	ST
10	B_2	—	—	—	—	—	—	0·05	0·05	—	—	0·67	—	0·1	0·05	5·0	5·0	ST
11	B_2	—	0·05	0·3	—	—	—	0·2	ST									
12	B_2	—	—	0·3	0·3	0·3	0·1	0·3	ST									
13	B_2	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	ST	
14	B_2	2·0	1·7	2·0	60·0	5·0	0·6	ST										
15	B_2	0·05	0·3	—	0·4	0·1	0·3	ST										
Luo With Sickle-cell Trait																		
1	M_1 B_2	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	ST
2	M_1 B_2	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	,,
3	M_1 B_1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	,,
4	M_1 B_1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	,,
5	M_1 B_1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	,,
6	M_1 B_1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	,,
7	M_1 B_1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	5·0	0·5	,,
8	M_1 B_1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	,,
9	M_1 B_1	0·7	—	—	—	—	—	—	—	—	—	0·03	0·1	0·03	0·03	—	—	,,
10	M_1 B_1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	,,
11	B_2 M_2	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	,,
12	B_2 M_2	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	,,
13	B_2 M_2	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	,,
14	B_2 M_2	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	,,
15	B_2 M_2	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	,,

Figures represent parasite counts in hundreds per mm.³ of blood. ST=Stopped by chemotherapy.

tion. Only two of the cases show parasites, and the parasite counts in these cases are comparatively low. The striking difference in the progress of malarial infection in the two groups is taken as evidence that the abnormal erythrocytes in individuals with the sickle-cell trait are less easily parasitized than are normal erythrocytes.

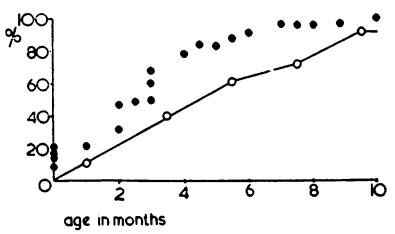
It can therefore be concluded that individuals with the sickle-cell trait will, in all probability, suffer from malaria less often and less severely than those without the trait. Hence in areas where malaria is hyperendemic children having the trait will tend to survive, while some children without the trait are eliminated before they acquire a solid immunity to malarial infection. The protection against malaria might also increase the fertility of possessors of the trait. The proportion of individuals with sickle cells in any population, then, will be the result of a balance between two factors; the severity of malaria, which will tend to increase the frequency of the gene, and the rate of elimination of the sickle-cell genes in individuals dying of sickle-cell anaemia. Or, genetically speaking, this is a balanced polymorphism where the heterozygote has an advantage over either homozygote.

The incidence of the trait in East Africa has recently been investigated in detail (Allison, 1954), and found to vary in accordance with the above hypothesis. High frequencies are observed among the tribes living in regions where malaria is hyperendemic (for example, around Lake Victoria and in the Eastern Coastal Belt), whereas low frequencies occur consistently in the malaria-free or epidemic zones (for example, the Kigezi district of Uganda; the Kenya Highlands; and the Kilimanjaro, Mount Meru, and Usumbara regions of Tanganyika). This difference is often independent of ethnic and linguistic grouping: thus, the incidence of the sickle-cell trait among Bantu-speaking tribes ranges from 0 (among the Kamba, Chagga, etc.) to 40% (among the Amba, Simbiti, etc.). The world distribution of the sickle-cell trait is also in accordance with the view presented here that malarial endemicity is a very important factor in determining the frequency of the sickle-cell trait. The genetical and anthropological implications of this view are evident.

The fact that sickle cells should be less easily parasitized by plasmodia than are normal erythrocytes is presumably attributable to their haemoglobin component, although there may be other differences, not yet observed, between the two cell-types. Sickle-cell haemoglobin is unlike normal adult haemoglobin in important physico-chemical properties, notably in the relative insolubility of the sickle-cell haemoglobin when reduced (Perutz and Mitchison, 1950). The malaria parasite is able to metabolize haemoglobin very completely in the intact red cell, the haematin pigment remaining as a by-product of haemoglobin breakdown (Fairley and Bromfield, 1934; Moulder and Evans, 1946). That plasmodia are greatly affected by relatively small differences in their environment is suggested by their remarkable species specificity. Thus the difficulty of establishing an infection in monkeys with human malaria parasites, and vice versa, is generally recognized.

How far species differences in the haemoglobins themselves, known from immunological and other studies, are responsible for the species specificity of plasmodia it is impossible to say. However, the physico-chemical differences between human adult haemoglobin and monkey haemoglobin appear to be less pronounced than the differences between either type and sickle-cell haemoglobin. It is clear that the natural resistance to malaria among individuals with the sickle-cell trait is relative, not absolute. This is perhaps attributable to differences in the expressivity of the sickle-cell gene, which may be responsible for the production of from nearly 50% to only a very small amount of sickle-cell haemoglobin (Wells and Itano, 1951; Singer and Fisher, 1953). Moreover, the sickle-cell haemoglobin may not be evenly distributed in the cell population: most observers recognize that there are cases in which only some of the red cells are sickled even after prolonged reduction. However, even a relative resistance to malaria may be enough to help those with the sickle-cell trait through the dangerous years of early childhood, during which an active immunity to the disease is developed.

The above observations focus attention upon the importance of haemoglobin to plasmodia in the erythrocytic phase. Hence it is worth considering whether erythrocytes containing other specialized or abnormal types of haemoglobin might be resistant to malaria also. Thus, human foetal haemoglobin differs from human adult haemoglobin in many properties. Red cells containing foetal haemoglobin continue to circulate in the newborn for the first three months of life, after which they are quite rapidly replaced by cells containing normal adult haemoglobin. It has long been known that the newborn has a considerable degree of resistance to malarial infection: Garnham (1949), for instance, found that in the Kavirondo district of Kenya at the end of the second month of life only 10% of babies were infected; after this age the percentage affected rises rapidly, until by the ninth month practically all children have the disease. The correspondence between the appearance of cells containing normal adult-type haemoglobin and malarial susceptibility is illustrated in the Chart. The correspondence may of course be fortuitous, but it is striking enough to merit further investigation, even though other factors, such as a milk diet deficient in *p*-aminobenzoic acid (Maegraith *et al.*, 1952; Hawking, 1953) and immunity acquired from the mother (Hackett, 1941) may play a part in the natural resistance of the newborn to malaria.



The apparent relationship between the appearance of adult-type haemoglobin (dots) and malarial infection (circles) in the newborn. Each dot represents a test on a single individual, using an alkali denaturation technique (Allison, unpublished observations); the circles represent the percentage of Luo children showing malaria parasites (Garnham, 1949).

Finally, it is possible that the explanation offered above for the maintenance of the sickle-cell trait may also apply to thalassaemia. The problems presented by the two diseases are very similar; many homozygotes, and possibly some heterozygotes, are known to die of thalassaemia, and yet the condition remains remarkably common in Italy and Greece, where as many as 10% of the individuals in certain areas are affected (Bianco *et al.*, 1952). Greek and Italian authors have commented that cases of thalassaemia usually come from districts severely afflicted wtih malaria (Choremis *et al.*, 1951). Perhaps those who are heterozygous for the thalassaemia gene suffer less from malaria than their compatriots: the fertility of the heterozygotes appears to be greater (Bianco *et al.*, 1952). Selective advantage of the heterozygote with the sickle-cell gene, and possibly the heterozygote with the thalassaemia gene also, would explain why such high gene frequencies can be attained in the case of these conditions while other genetically transmitted abnormalities of the blood cells remain uncommon, not very much above the estimated mutation rate—for example, hereditary spherocytosis (Race, 1942).

Summary

A study has been made of the relationship between the sickle-cell trait and subtertian malarial infection. It has been found that in indigenous East Africans the sickle-cell trait affords a considerable degree of protection against subtertian malaria. The incidence of parasitaemia in 43 Ganda children with the sickle-cell trait was significantly lower than in a comparable group of 247 children without the trait. An infection with *P. falciparum* was established in 14 out of 15

Africans without the sickle-cell trait, whereas in a comparable group of 15 Africans with the trait only 2 developed parasites.

It is concluded that the abnormal erythrocytes of individuals with the sickle-cell trait are less easily parasitized by *P. falciparum* than are normal erythrocytes. Hence those who are heterozygous for the sickle-cell gene will have a selective advantage in regions where malaria is hyperendemic. This fact may explain why the sickle-cell gene remains common in these areas in spite of the elimination of genes in patients dying of sickle-cell anaemia. The implications of these observations in other branches of haematology are discussed.

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In 1950 a mass-miniature-radiography survey was undertaken in Los Angeles County, California. The population concerned numbered over three million, and more than half —1,736,703—responded and were *x*-rayed satisfactorily. This was the largest survey undertaken up to that date in the United States. Abnormalities were found in 67,966 individuals, of whom ultimately 2,404 were classified as tuberculosis suspects. 1,857 previously unknown cases of active tuberculosis were discovered—a rate of 1.08 per 1,000. Among 10,899 cardiovascular suspects the diagnosis of heart disease was confirmed in 3,388, but of these only 697 were previously unknown : the discovery rate for cardiac cases was 0.4 per 1,000. Exactly 3,500 lung cancer suspects were registered. Ultimately neoplasms were confirmed in 329 cases, of which 246 or 0.14 per 1,000 were malignant. (*Los Angeles County-wide Chest X-ray Survey of 1950*, by G. J. Drolet. Published by the Tuberculosis Control Foundation, Los Angeles, 1953.)

THE VARIABILITY OF SICKLE-CELL RATES IN THE TRIBES OF KENYA AND THE SOUTHERN SUDAN

BY

HENRY FOY, M.A., Ph.D., D.Sc.

ATHENA KONDI, M.D.
Wellcome Trust Research Laboratories

G. L. TIMMS, M.B., B.S.
Kenya Medical Service

W. BRASS, B.Sc.
East African Statistical Department

AND

FARDIL BUSHRA, M.D.
Principal Medical Inspector, Sudan Government

We have recently completed a survey of the distribution of sickle cells in the blood of 44 tribes and subtribes in Kenya, and 26 in the southern provinces of the Sudan. The results are given in Tables I and II. In a certain number of tribes the ABO blood groups were also done, the results being given in Table III.

In the present communication we wish to stress that, while the sickling phenomenon is very widespread throughout Africa, south of the Sahara the most striking

TABLE I.—*Sickle-cell Trait (Kenya)*

Race	Tribe	Tribal Division	Location	No. Examined	Positive No.	Positive %
Bantu (North-East, Coastal)	Kikuyu	Fort Hall	Nairobi	67	1	2
" "	Teita	Dabida	Wesu	127	0	0
" "	Pare		Taveta	40	2	5
" "	Chagga		Kibo	75	0	0
" "	Taveta		Taveta	154	37	24
" "	Kamba		Machakos	134	2	1
" "	Nyika	Giriama	Malindi	150	16	11
" "	"	"	Ganda Kilifi Jaribuni	39	4	10
" "	"	Kauma				
" "	"	"				
" "	"	Chonyis	Kaloleni	90	23	26
" "	"	Jibanas	"	119	16	13
" "	"	Rabais	Rabai	48	5	10
" "	"	Ribe	Ribe	50	13	26
" "	"	Kambe	"	78	27	35
" "	"	Digos	Msambweni	50	11	22
" "	"	Durumas	"	68	7	10
" "	Pokomos	Ngatana	Garsen	102	27	27
" "	Boni		Bargoni	81	0	0
" "	Sanya		Witu	61	0	0
" "	"		Adu	68	8	12
Bantu (North Kavirondo)	Maragoli		Majengo	100	9	9
" "	Bunyori		Kimba	100	6	6
" "	Nyangori		Kapsengeri	44	2	5
" "	Kitosh		Bungoma	100	21	21
" "	Kakamega		Kakamegas	50	6	12
" "	"		"	46	0	0
" "	Marama		Buteri	100	10	10
" "	Wangas		Mumias	96	19	20
" "	Kisii (Bantu-Nilote?)		Kericho	100	3	3
Bantu (South-East, Coastal)	Makonda		Porto Amelia	100	40	40
" "	"		Vipinco	50	2	4
E. Hamites	Masai	Kaputei Lodokelani	Kajiado	100	0	0
" "	"	Purko Loita	Narok	82	0	0
" "	Galla		Garsen	30	0	0
" "	Kipsigis		Kericho	100	2	2
" "	Somalis	Adjuran		14	0	0
" "	"	Degodia		20	0	0
" "	"	Ogaden		16	0	0
" "	"	Gurren				
" "	Boran	Sakuya		6	0	0
Nilo-Hamites	Turkanas			50	0	0
Nilotes	Luo	S. Kavirondo		100	28	28
Mixed Arab–Negro	Bajuns	Lamu		45	1	2
" "	Swahili	Ganda		50	2	4
" "	"	Kakounyi		50	5	10
" "	Arabs	Malindi		61	1	2